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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,816	11/04/2003	Zuoshang Xu	UMY-038	9864

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EXAMINER	
MCGARRY, SEAN	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,816	XU ET AL.	
	Examiner	Art Unit	
	Sean R. McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 21-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 21-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/16/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of Group I in the reply filed on 7/10/2006 is acknowledged. Applicant has canceled all claims drawn to the inventions of groups III and IV and notes that groups I and II are linked by claim 1 and that the restriction depends on the nonallowability of claim 1. The restriction between groups I and II, however has been withdrawn as far as the claim are now presented. The search for Group I provided an adequate search for the examination of Group II as well. The restriction requirement between Groups I and II is withdrawn since the claimed inventions, as now presented, do not present a large burden for examination.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Davidson et al [US 2005/0106731].

Davidson et al disclose the use of siRNA to silence gene alleles involved in ALS and Huntingtons. See paragraphs [0100], [0106] and claim 52, for example.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 and 21-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davidson et al [US 2005/0106731], Klug et al [European Journal of Physiology, Vol. 441 (6 Suppl): R205, 2001], Brown et al [WO 94/19493], Siddique et al [Neurology Vol. 47(suppl 2): S27-S35, 1996], and Kunst et al [Nature Genetics Vol. 15: 91-94, 01/15/96].

The instant invention is drawn to the inhibition of a targeted specified allele in a cell via siRNA. The invention is more specifically drawn to dominant gain of function

alleles of specified diseases and to specified alleles and to the use of specific siRNA and shRNA targeted to specific ALS alleles.

Davidson et al have taught throughout their specification how to make and use siRNA and shRNAs to inhibit targeted genes in mammalian cells and for their use in the treatment of disease including expression from vectors. Davidson et al have specifically asserted the targeting of genes involved in ALS, Huntingtons disease, Alzheimers disease, and Parkinsons disease (see paragraph [0106]). Davidson et al have taught that the siRNAs and shRNAs of their invention can be used to target specific alleles for the specific silencing of one allele of a gene [see paragraph 0100], for example).

Davidson et al have not specifically disclosed the targeting of a specified mutation in the treatment of disease.

Brown et al have taught the involvement of SOD1 and in particular specific mutations in SOD1 that lead to dominant gain of function ALS (see page 28, for example). At pages 10, 31, 53, and claims 43-45 and 47, for example) it is taught to inhibit mutant SOD1 via antisense. In Tables 3A and 3C, the specific mutations targeted by the instant invention are disclosed [G256C and G281C which correspond to G85Arg and G93A].

Klug et al have taught the targeting of the most common SOD1 mutant gain of function allele G93A with antisense. It was shown the selective inhibition of the mutant allele and uptake of antisense in the brain.

Siddique et al have disclosed SOD1 mutations associated with ALS (see Table, for example).

Kunst et al have also shown that the specific mutant alleles for SOD1 associated ALS were well known at the time of invention (see Figure 1, for example.

The prior art has therefore shown that SOD1 dominant gain of function mutants are causative for ALS. The prior art has shown the targeted inhibition of specific SOD1 alleles via antisense.

The prior art has taught that siRNA and shRNA can be used to specifically target a desired allele of a gene.

The prior art has shown that mutations associated with ALS (SOD1 have been known for some time before the instant invention. The prior art has also taught to target the mutant alleles of SOD1 selectively over the wt. Since the prior art has also asserted the usefulness of siRNA and shRNA for treating ALS it would have been obvious to use them since the prior art has shown that such targeting was successful using antisense. Davidson et al have provided extensive guidance for making siRNA and shRNA and since the sequence of SOD1 and more importantly since the specific mutant sequences were known and the art clearly suggest targeting them, the siRNA and shRNA sequences of the instant invention are merely optimizations at best.

The invention as a whole would therefore have been *prima facie* obvious at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean R McGarry
Primary Examiner
Art Unit 1635